Written evidence from AstraZeneca (ENB0044)

Contents

What does AZ think overall of the government's Strategy on Engineering Biology published in November 2023

- **AstraZeneca welcomes the government's current focus on science and R&D.** We were not aware of how Engineering Biology was selected as one of DSIT's (and the UK's) top 5 areas of focus, alongside AI, Quantum, etc, but we are not opposed per se to this Engineering Biology being supported. We strongly welcome the government's stated commitment to a longer-term, 10-year strategy, this is brilliant, it creates reassurance and stability for researchers and investors, and also improves the attractiveness of the UK as a research location.

- **AstraZeneca welcome the Engineering Biology Strategy setting out six overarching objectives to strengthen the UK ecosystem:** 1. World-leading R&D; 2. Infrastructure; 3. Talent and skills; 4. Regulation and standards; 5. Adoption in the wider economy; 6. Responsible and trustworthy innovation. We believe these are valuable foundations for science. **However, these are of course also set out in a number of other Government Strategies –** from the DSIT Framework, in the Life Science Vision, and in part within many other reviews such as the Harrington Review, etc. We do not see how they are linked up or connected to deliver together. We hope that there is not a duplication of effort or waste of resource, as each of these strategies is delivered.

- **We welcome government funding for science and R&D,** but were not aware of any consultation around the amount of funding being allocation to Engineering Biology, nor the exact rationale, as discussed below. We see that £100m funding via UKRI has already been allocated to 22 projects, each with quite specific research interests. We would imagine that for the £2 billion that will be

allocated over 10 years as announced, going forward there would be more consultation on its allocation.

- **Does the UK need more early-stage research?** The UK has world-renowned, even world-leading R&D, and the major issue for the UK on life sciences are the hurdles and pitfalls in commercialisation and generating value beyond the lab/academia. The government and DSIT in particular have stated that they want to grow the sector by supporting scale-up and growth, but the Engineering Biology £100m funding went towards academic/early stage research. The UK risks staying in the famous "valley of death" before growth, and losing out to the US and other competitors, who are supporting their life science sectors to grow and commercialise – which generates a skilled workforce, jobs, manufacturing, attracts further investment, and really delivers for the wider economy and public.

- **The Strategy sets out some UK strengths, but does not appear to have specific criteria of what is included in or meant by "Engineering Biology".** AstraZeneca are hopeful that this will be discussed and defined by the Steering Board that is being set up. An expert board will be able to advise areas of "Engineering Biology" that would for example generate maximum ROI; or which could put the UK in a world-leading position.

- **We would expect the Engineering Biology to set out a Delivery Plan. We can already see a "delivery plan" by proxy** – we can see the type of projects being funded by the £100m fund, so in a retrospective way this is a strategy of sorts. There are four focus areas with 2-8 projects funded for each: 4 projects on food systems; 8 projects on biomedicine; 8 projects on clean growth; 2 projects on environmental solutions. It is not clear how this was decided – for example is environmental solutions less important hence only 2 projects? Which projects were not chosen, and why? It would be better to see this articulated in a delivery plan upfront.

- **What does "success" look like for the Strategy?** It will be vital to define success, to determine end points, to review ROI, and to make any logical and evidence-based decisions on subsequent funding rounds, We would expect this to be consulted on. It would

be great to have this aligned with outputs or goals set out, which the funding and research can then address.

Which areas in the Strategy would AZ want to engage on?

- **Disclaimer: AstraZeneca have just joined the Engineering Biology Steering Board.** In AstraZeneca we are committed to R&D and we invest over £2bn per year in the UK and we have core strengths in Engineering Biology in particular novel methodology and technologies to transform disease. AstraZeneca see great value in the partnership between government, research and industry, and due to our engagement across government we can identify how government policy on AI, data, and genomics can all also drive forward Engineering Biology. We are supportive and keen to ensure that government funding and policies have more impact than the sum of their parts, in particular to pull R&D benefits across from the lab and academia right through to delivering for the economy and public.

- **AstraZeneca welcome "Health" being one of the five sectors selected.** Health research has obvious proven benefits for the economy and the public, not least of all demonstrated over the pandemic.

- **We would expect the Strategy to set specific goals or outcomes on Health, and even to articulate how this will make the UK world-leading.** As it stands, the Health section in the strategy lists a selection of areas where the UK has strengths, we of course agree with this but it is not very strategic. (For info the areas listed are - personalised therapies such as CAR-T cancer therapy; artificial organs and smart drugs; mRNA vaccines and therapies; diagnostics in Precision Medicine and targeted immunotherapies).

- **To flag, the Missions (the 8 projects) funded via UKRI on Health (aka biomedicine) do not address nor relate to the Health areas outlined in the Strategy. We would expect funding on the areas highlighted, including personalised medicine such as CAR-T therapy, etc.** Rather the funding is so far allocated to very early-stage cellular biology – SEE ANNEX. Whilst this is indeed a foundation for engineering biology, we would

expect some more directly applicable outputs, or disease focus, in particular to prevalent long-term conditions in the UK, for these projects to generate genuine direct benefit to the UK.

- **Overall, we would expect any funding allocated, to ultimately benefit the entire UK R&D ecosystem, and we would hope for this to be articulated in the Strategy.** We would therefore expect the research that was funded by £100m from UKRI to lead to UK-wide benefits on engineering biology. This could work on a number of levels, for example the R&D, data, findings, and technological methods, could be shared across the UK; or the outputs from the research could be commercialised to directly benefit the UK economy and public; or any subsequent innovation could be grown as a UK company, anchored in the UK and this could create jobs and stimulate further growth of the ecosystem and economy (instead of say, research being spun off and bought by a foreign investor).

Should the Strategy be extended? What are the applications and outcomes?

- **In AstraZeneca we are designing new ways to target the drivers of disease** to help us create the next generation of therapeutics, going beyond traditional small molecules, monoclonal antibodies and peptides. The diversity of technologies applied in our early pipeline is exemplified by the increased number of new modalities entering clinical development, and 30% of our early pipeline now consists of new drug modalities, including oligonucleotides, mRNA, bicyclic peptides and Anticalin proteins.

- Key areas of interest to AZ within engineering biology include:
    - **Next generation cell therapies** – in AZ we make sure that we are at the cutting edge of novel therapies, which you can see from our R&D, our business activity, and is evidenced in a significant portion of our pipeline representing novel modalities!
    - **Refining technologies to deliver advanced therapeutics**, including refining the power of gene editing to target specific sites in the body and thereby unlock potential curative therapies.

- **Convergence of synthetic chemistry and recombinant biologics**, including synthetic antibodies, in vivo expressed biologics, and more.
- **Harnessing the application of ML and AI across** drug discovery workflows, which we already do, but we can capitalise on this to predict cellular function, to identify novel drug targets and disease mechanisms, and to use in silico methods to design novel therapeutic molecules – and this of course has applications far beyond the life sciences.
- **Manufacturing for the biotech and life sciences sector** – including technology development as it applies to cell-expressed products, as well as aspects of biocatalysis and green chemistry.

What should the UK Government do to help EB?
Should there be any Regulation? Are there any Risks?

Some initial suggestions of how Government support would be best directed include:

- **Support for Cell Therapies;** encourage close alignment between clinical research hospitals and industry to create centres of excellence in cell therapy manufacture and application.
- **Training;** consider how traditional sciences/engineering are taught – integrating principles from the tech sector, such as data handling and ML, from an early stage.
- **Grand Challenges:** the government should consider setting up Grand Challenges that encourage interdisciplinary collaboration in areas like synthetic biology, cross-modality drug discovery...

On risks - getting the balance of IP vs knowhow/trade secret right in areas such as manufacturing. In addition, considering how generative AI and rapid ML based optimisation might make UK innovation more vulnerable.

ANNEX I

UKRI FUNDED PROJECTS:

Rosser Lab

Developing tools for synthetic biology approaches for pathway and genome engineering in bacteria, yeast and mammalian cell systems. The applications of her work include rapid strain engineering for production of high value secondary metabolites, cell lines for protein production, engineering bacteria to generate electricity and developing genetic tools for bio-computation: engineering cells to sense, process and memorise information.

Heap Lab

Glycans have a huge impact on biology, are integral to the way that our immune system interacts with pathogens, and ensure that many modern pharmaceuticals function properly. However, glycans are currently very difficult to study and manufacture and can be considered to be the "dark matter" of biology. The GlycoCell Engineering Biology Mission Hub will bring together a range of experts from different fields to unlock the potential of glycans. This promises to accelerate vaccine discovery and production, generate new therapeutics and diagnostics, and dramatically reduce the production costs of advanced drugs.

Vllasaliu Lab

Driton's research interests centre around overcoming the biological barriers to improve drug delivery and enable non-invasive delivery (e.g. oral) of drugs that currently require administration by injections. As part of this, he has specific interests in drug delivery systems, including nanomedicines (he was awarded an EPSRC 'First Grant' in this area), for mucosal delivery. He is also interested in drug delivery in mucosal diseases (e.g. Inflammatory Bowel Disease) and how such diseases influence drug absorption and delivery. Finally, aspects of Driton's research relate to the creation of improved (more predictive) in vitro mucosal models for use in drug discovery and delivery research. The overarching aim of Driton's activity is to improve patient outcomes through translational drug delivery research.

Nolan Lab

1 - Genetic control of mosquito populations in order to control malaria transmission
2 - Development of functional genetics tools for the study of key mosquito traits (such as insecticide resistance, mosquito fertility, bloodmeal

digestion etc.)
3 - Developing and sharing capacity around the molecular biology and genetics - both knowledge and practical infrastructure - that is needed to accompany the implementation and monitoring of vector control programmes

Berger-Schaffitzel Lab

Our team studies the function and structure of NMD factors using biochemistry, biophysics and structural biology.

Nonsense-mediated mRNA decay (NMD) represents a key surveillance mechanism to quality control the expression of normal and aberrant mRNAs in eukaryotes. NMD recognizes and degrades transcripts with premature termination codons (PTCs), NMD limits the production of potentially harmful, C-terminally truncated proteins. NMD thus represents one of the main quality control mechanisms of the eukaryotic cell. In addition, NMD is an important regulator of overall eukaryotic gene expression.

Itzhaki Lab

"MAST, modular activator and silencer therapeutics" project. Our research focuses on a class of proteins with very distinctive architectures, known as tandem-repeat proteins. Our group and others have shown that the simple modular, one-dimensional architecture of tandem-repeat proteins gives them distinctive properties that make it uniquely straightforward to map the energetics of their structures and to rationally redesign their stability, folding and binding function. This class of proteins is thus an exceptionally sensitive and versatile tool that we are now exploiting to dissect otherwise intractable cellular mechanisms. We are also exploring how to exploit the extraordinary design-ability of these proteins for biomedical and biotechnology applications.

Watson Lab

"Synthetically engineered microalgae for improved gut function and human health" project. My research interests range from exploiting bioenergy and microalgae, laser asteroid deflection and laser and combined systems for inactivation of microorganisms. Areas permeating each theme are complex experimentation, real time detection, monitoring and control of processes.

Thomas Lab

"Evaluation and optimisation of new engineered human apoferritins: protein nanocages for targeted drug delivery and intracellular cargo

release" project. His current research interests are in the identification of inhibitors of enzymes essential to Mycobacterium cell wall biosynthesis; synthesis of mechanistic probes based on Coenzyme A, S-adenosylmethione, ATP and biotin; use of enzymes in unusual reaction media (fluorous biphasic systems; supercritical fluids); development of enzyme-based antimicrobial therapies; development of enzyme-activated magnetic resonance imaging (MRI) agents; development of in vivo probes based on quantum dots and protein capsids; healthcare applications of self-assembling proteins including apoferritin and spider silk.

Colley Lab

"Electrospun mucoadhesive matrices for polymersome-mediated mRNA vaccine delivery" project. My current research combines my interests in tissue-engineering and epithelial biology where I supervise a range of translational and interdisciplinary research projects. I teach Human Anatomy to Dental and Speech Therapy students at both undergraduate and postgraduate level.

Darlington Lab

"Optimal cell factories for membrane protein production" project. Our group aims to tackle roadblocks to industrialization of synthetic biology by developing quantitative mathematical models that can inform and guide the engineering of biological systems. We develop models which combine metabolism, gene expression and microbial growth to understand how these multiple dynamic constraints emerge over the course of population growth during industrial production processes and how they impact the function of engineered gene circuits and pathways. Our group works closely with experimental colleagues to validate model predictions in vivo and implement the new design strategies we identify.

ANNEX II

House of Lords Science and Technology Committee
Call for Evidence on Engineering Biology
https://committees.parliament.uk/call-for-evidence/399

Questions:

1. **What are the UK's key strengths in the area of engineering biology?**

a. Notable research institutes or groups
b. What is the current economic impact?

2. What are the key applications for engineering biology?

a. Examples of particularly exciting or interesting applications
b. Timescales?
c. Expectation vs reality?
d. Added value over current processes?
e. Comparison with other countries?

3. How can Government policy support EB?

a. Does the Government's "National Vision for Engineering Biology" set out the right priorities?
b. Was there anything missing?
c. The Government has committed to spend £2 billion over the next 10 years on engineering biology. Is this scale of subsidy sufficient to be competitive? Where should this funding be focused?
d. What should the role of UKRI be?
e. Which Government departments, and non-departmental public bodies, are engaged or should be engaged?
f. Which are the key recent enabling technologies?
g. Is the UK getting the best value out of its existing facilities?

4. How can the UK maximise the economic potential of EB?

a. Who is investing in engineering biology in the UK?
b. How should the Government best support EB startups to scale-up in the UK?
c. How well are Innovate UK, the British Business Bank and British Infrastructure Bank supporting the commercialisation of engineering biology?

d. Are there any elements of UK taxation policy which could support? How does it fit into efforts to increase investment in UK technology companies, such as the Mansion House reforms?
e. Are there opportunities for engineering biology to be used to improve public services, or public procurement opportunities?
f. Where could engineering biology improve productivity (GDP/capita) or GVA?
g. Does the UK need large companies in the field?
h. Should the UK focus on bulk materials or chemical production, or high-value-add but relatively low through-put applications?
i. What can the Government do to encourage investors?
j. How does the UK's approach to engineering biology, commercialisation and translation compare to other nations, such as Germany, China and the US?
k. Could UK EB be exploited overseas?

5. What are the risks posed by EB?

a. What are the major regulatory, ethical, and safety concerns?
b. Does EB pose national security risks? Is the Government's 2023 Biosecurity Strategy sufficient?
c. What early warning systems are in place to monitor whether engineering biology is being misused? Is further regulation needed, for example setting out what DNA synthesis technology can be used for?

6. How should engineering biology be regulated?

a. Who regulates engineering biology in the UK and internationally?
b. Is the current regulatory framework adequate?
c. How are the ethical, safety, and national security concerns addressed?
d. How would rapid progress impact regulatory structures, e.g. IP?

e. Has regulation in this area evolved quickly enough? What should the Government do to ensure the regulatory environment is able to keep up?
f. Is there a tension between the desire to support open-access science – for example in genome sequencing, genetic datasets, engineering biology platforms and techniques – and a risk that IP developed in the UK is exploited elsewhere?

7. What are the possible barriers and limitations to good and effective use of engineering biology? What is already known about the likely limitations of engineering biology due to limits in our scientific understanding?

a. What more can the Government do to foster public understanding
b. Does the UK have a sufficient skills base to harness the potential of engineering biology?
c. What barriers are there to incumbent manufacturers making use of engineering biology techniques? Is there anything the Government can do to address these?
d. What are some of the key feedstocks and enabling technologies?
e. Does lack of land (e.g. for biofuels or growing GM crops) or dedicated lab space inhibit the growth of engineering biology?

ANNEX III

BACKGROUND to the Engineering Biology Strategy

- The government's Engineering Biology strategy was published in Dec 2023, by the Department for Science Innovation and Science.

- **The Government's vision is for the UK to have a broad, rich engineering biology ecosystem that can safely develop and commercialise.** The aim is to capture as much economic value, security, resilience and preparedness as possible from the UK's strengths and ensure these create real benefits for the public. This will be underpinned by public investment, supportive infrastructure, enabling regulation and standards, open markets, and a culture of responsible and trustworthy innovation.

- **The Strategy sets out six overarching objectives: 1**. World-leading R&D; 2. Infrastructure; 3. Talent and skills; 4. Regulation and standards; 5. Adoption in the wider economy; 6. Responsible and trustworthy innovation.

- **The government will set up a new Engineering Biology Steering Group.** Simon Chell from AstraZeneca has been accepted on the Group.

- **The government have committed to investing £2 billion over the next 10 years to deliver this vision.** £100m Funding for six new UK Research and Innovation (UKRI) Engineering Biology Mission Hubs and 22 Mission Award projects was announced in February 2024.
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- **The Strategy sets out 4 sectors:** (1) Health, (2) Agriculture and Food, (3) Chemicals and Materials, (4) Low carbon fuels, (5) National security, resilience and preparedness.

- **The Strategy acknowledges that the applications of engineering biology are highly diverse, but it lists common underlying technologies:** (1) the rapidly falling cost and access to DNA sequencing which allows for the assembly of large bioinformatic data sets; (2) the deployment of computational power, AI and machine learning on these datasets which allows

researchers to predict the relationship between DNA sequence, protein folding and, ultimately, protein functions; (3) the ability to write custom DNA sequences cost-effectively; (4) powerful gene editing techniques such as CRISPR-Cas9 can empower new innovations.

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